بسم الله الرحمن الرحيم

OUTLINE

- Definition
- Classification
- Clinical Features
- Lab abnormalities
- Diagnosis
- Lupus related syndromes

Lupus Erythematosus

- Autoimmune disease, Ch by auto-Abs to self nuclei" Immune complex deposition in CT,

-widespread inflammatory da

- Difficult to diagnose as

Symptoms &signs are nonspecific

- & tend to overlap.

Classification of cutaneous LE spectrum

Chronic cutaneous LE (DLE) I)

- Well defined scarring discoid lesions
- -ve serology
- More in females (2:1)
- No systemic lesions

1. Localized
2. Generalized
3. Hypertrophic
4. Lupus profundus
5. Erosive palmoplantar

Classification of cut. LE (Cont'd)

Subacute cutaneous LE (SCLE) II)

- Photosensitive non-scarring lesions
  - Annular polycyclic
    - or
  - Psoriasiform

  Heal with grey pig
- Mild systemic lesions (in 50%) mainly arthritis, but rare renal affection

Neonatal LE

- +ve anti-Ro & La Abs (70%)
- +ve ANAs
- -ve anti-nDNA, anti-Sm & anti-RNP
- More in females (3:1)

Classification of cut. LE (Cont'd)

Acute cutaneous LE (SLE) III)

- **Specific skin lesions**
  - Facial "malar" erythema
  - Discoid LE lesions
  - Photosensitive dermatitis
  - Generalized erythema
  - Bullous lesions (BSLE)
- **Severe multisystem affection &**
- **renal affection**

- +ve anti-nDNA,
- anti-Sm & low comple
  - +ve ANA
- More in females (8:1)

Classification of cut. LE (Cont'd)

Mixed connective tissue dis. (MCTD)

- Raynaud's phenomenon, sclerodactyly & arthralgia but rare renal affection

- +ve anti-nRNP Abs

Drug-induced LE

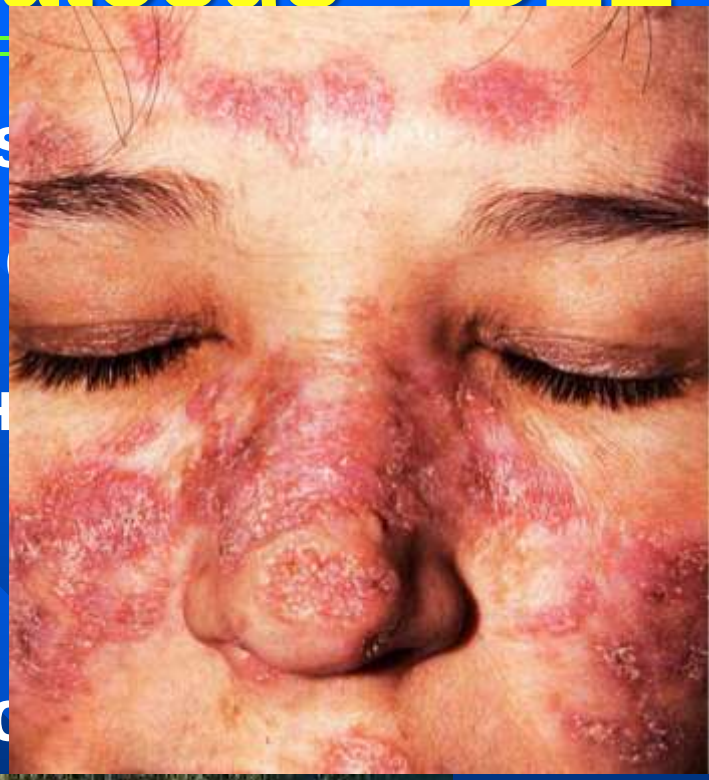
- +ve anti-histones Abs

Discoid lupus erythematosus – DLE

- erythematous, discoid plaques
  adherent scales & follicular plu
- Heal: thin, white atrophic scar +

raised or hyperpigm border.

- Neoplastic change (SCC or BCC

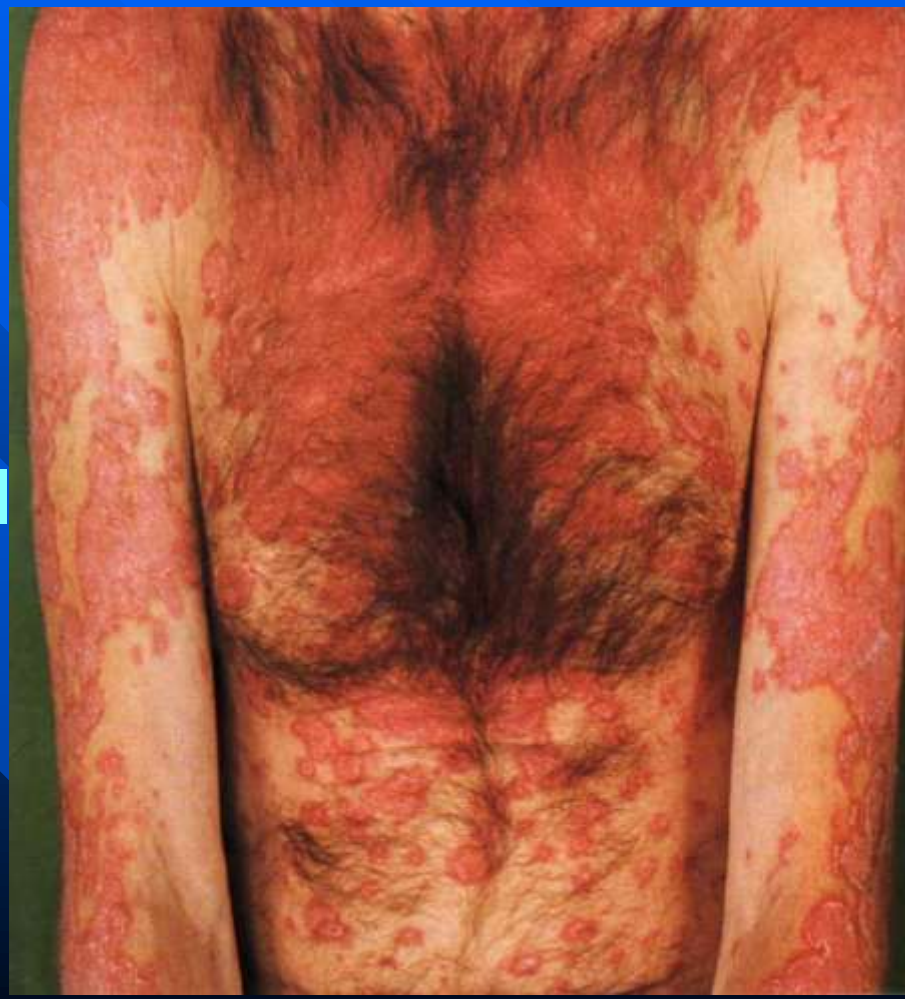


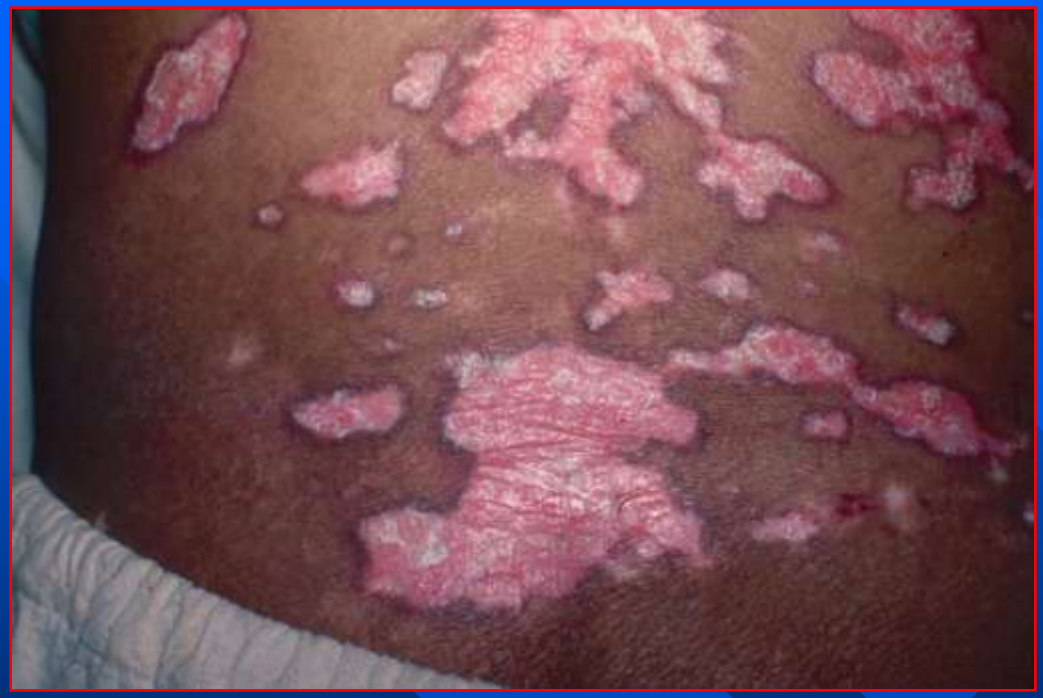
- Site: sun-exposed areas, -face (butterfly area),
- -scalp(cicatricial

Widespread DLE

Widespread – other areas than the head & neck.

- **Clinically: patients DLE**
- **Have a chronic course, less remission.**
- **Difficult to control.**
- **Frequent serol abnormalities**
- **& risk of cytopenia.**





- **High Photosensitivity, 50% meet criteria for SLE**

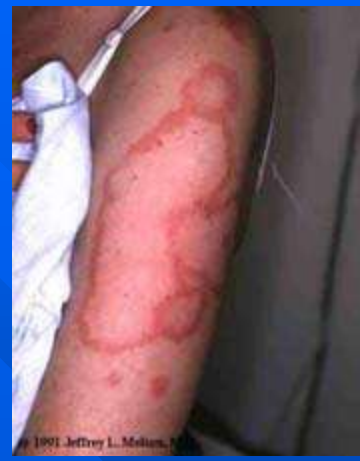
Subacute cutaneous lupus erythematosus (SCLE)

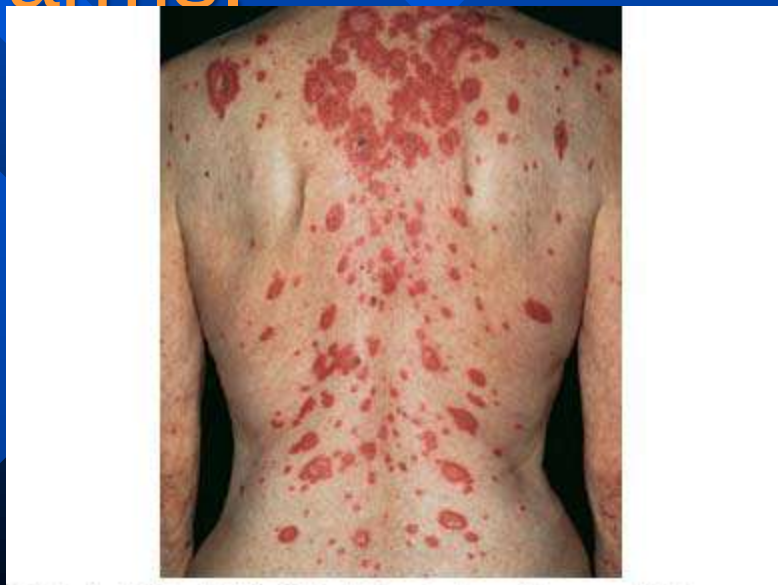
- **Anti-Ro+ (SSA+),**
  - **Variants: Annular erythematous variant**
  - **Psoriasiform variant**
  - Deficiency of C2 (2nd component of complement)

  - Associated phenomena
  - **Drug-induced SCLE**
  - Neonatal LE
  - **Sjogren's syndrome (Annular erythema)**

Subacute cutaneous LE (SCLE)

- Annular-polycyclic pattern +erythematous scaly border &hypopigmented centre,
- confined to back and arms.
- ANA +ve





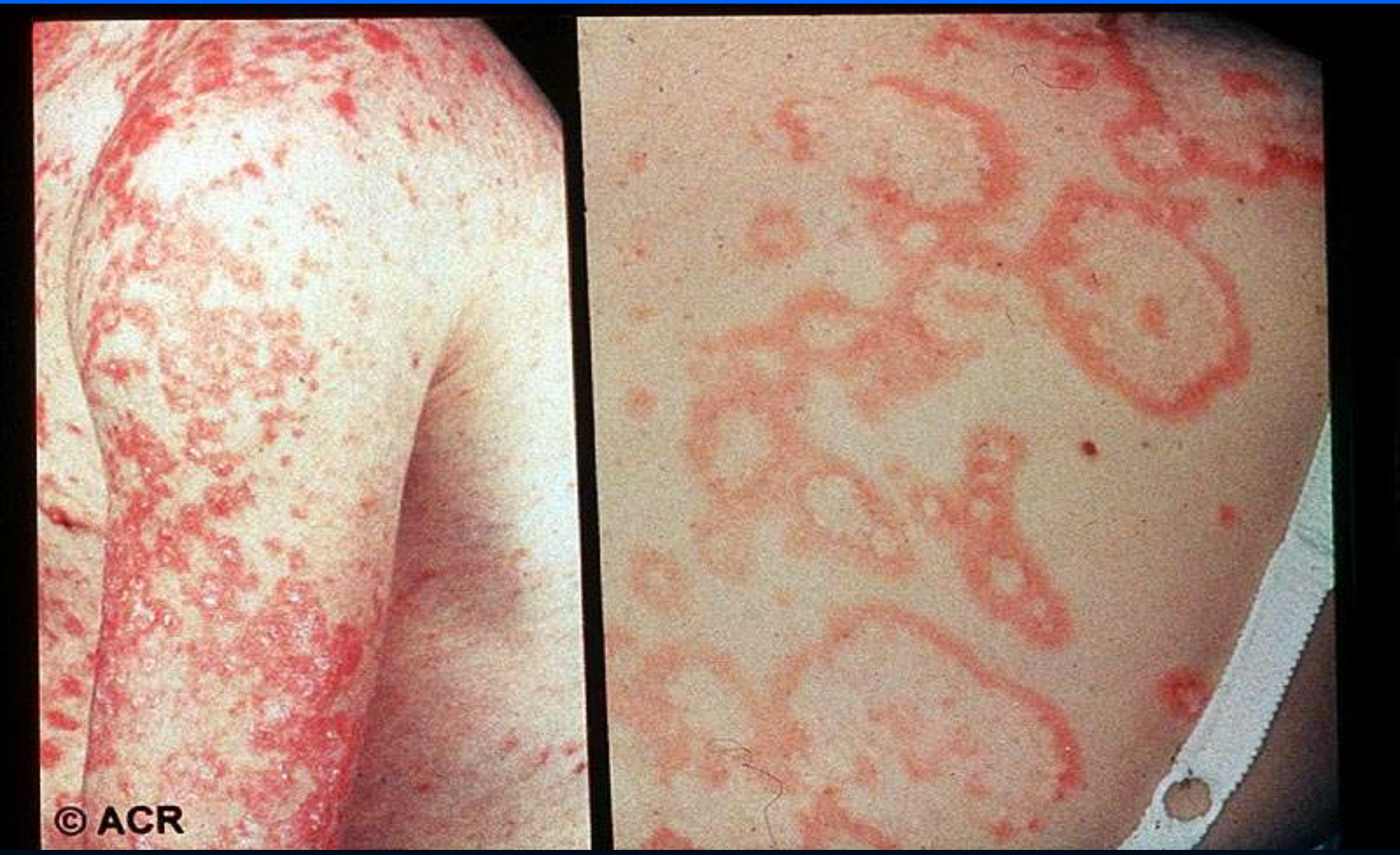
Anti-Ro antibody +ve lupus subsets

Clinical features

Cutaneous lesions

- Non-scarring annular or psoriasiform lesions.
- Photosensitivity.

Subacute Cutaneous Lupus



Anti-Ro Ab +ve lupus subsets (Cont'd)

- ***Mild systemic manifestations***
  - **Arthritis**
  - **Pulmonary diseases**
  - **Neuropsychiatric disorders**
  - **Vasculitis**
  - **Rare renal diseases**
- ***Increase incidence of HLA-DR3.***
- ***Good prognosis.***

Neonatal LE “NLE”

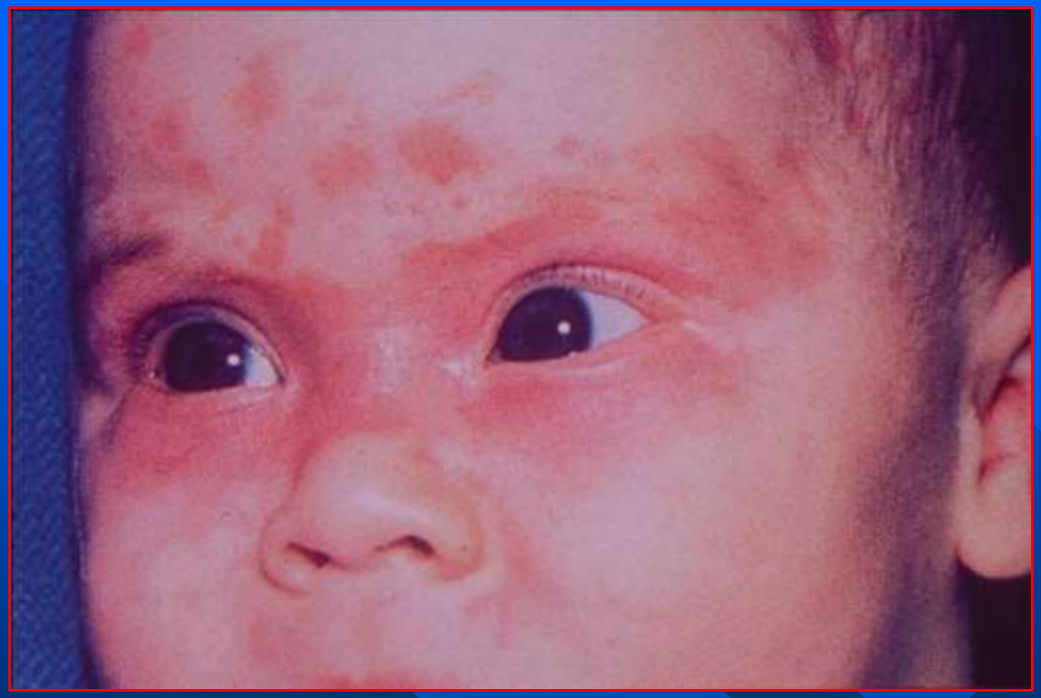
- It occurs in female infants of mothers(↑ prevalence of HLA-DR3 & B8) who have or will develop CTD.

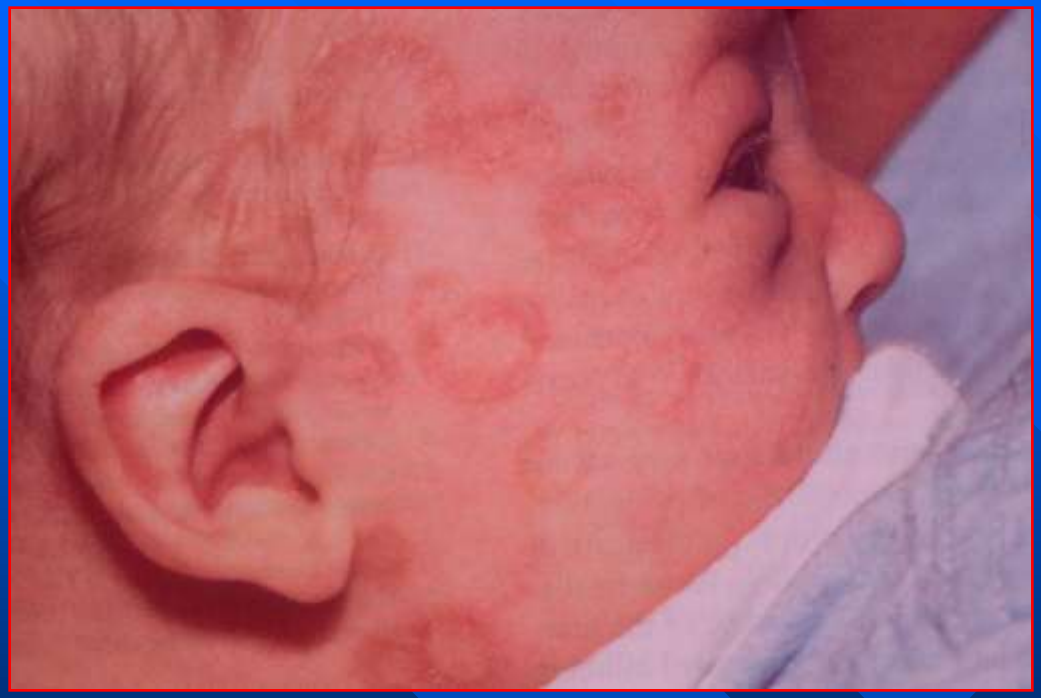
- Anti-Ro Abs “serological markers”.

- The infant develops:

- Periorbial “owl-eye”.
- SCLE-like lesions. Photosensitivity.

- Transient: thrombocytopenia & cholestatic hepatitis.





Neonatal LE "NLE" (Cont'd)

- **of babies Mothers with congenital heart disease have a 1:3 chance of developing SLE or other connective tissue disease.**

Acute cutaneous LE

(Systemic lupus erythematosus – SLE)

CLINICAL FEATURES:

- **Constitutional** 50-100% Fatigue, fever (in absence of infection), weight loss.
- **Musculoskeletal** 67% Arthritis, arthralgia, myositis
- **Hematologic** 36% Anemia, leukopenia, thrombocytopenia,
- **RES:** 7-23 % Lymphadenopathy, HSM.

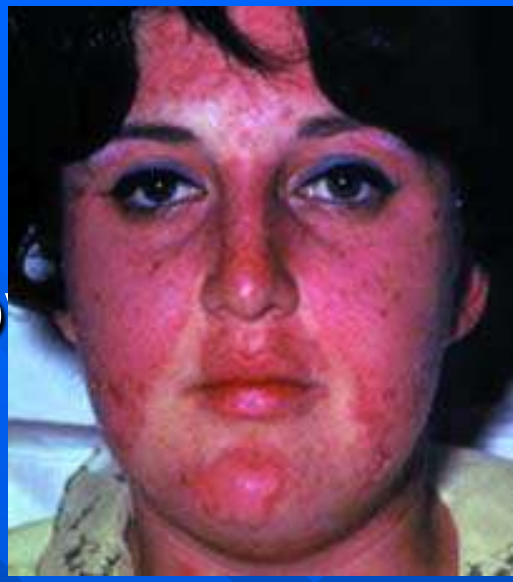
CLINICAL FEATURES:

- **Skin:** 73% Butterfly rash, photosensitivity rash, mucous membrane lesion ,alopecia, Raynaud's phenomenon, purpura, vasculitic ulceration, Nailfold capillary changes
- **Renal** 16-38% Hematuria, proteinuria, cellular casts, nephrotic syndrome

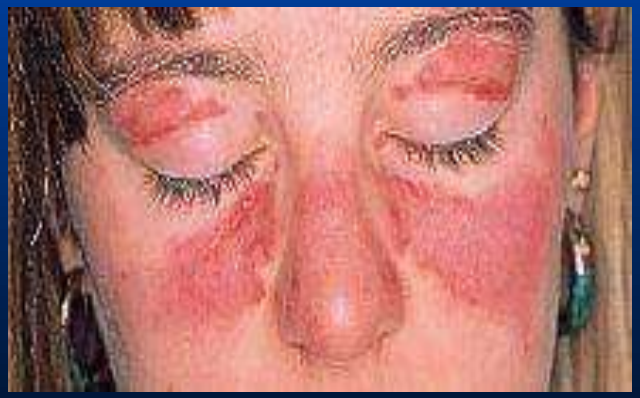
CLINICAL FEATURES:

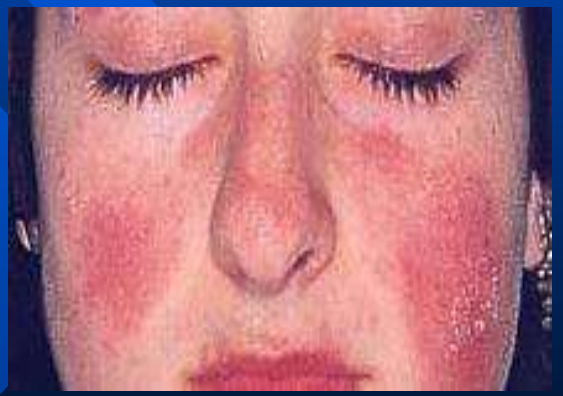
- **Neuropsychiatric** 12-21% Psychosis(Behavior/Personality changes, depression) ,cranial & peripheral neuropathies
- seizures, Chorea, Stroke
- **GIT:** 18 % Nausea, vomiting, abdominal pain
  - **Cardiac** 15 %: Pancarditis, Valvular orCoronary Artery Disease.
- **Pulmonary** 2-12 %: Pleurisy, pulmonary HT, pulmonary disease.

MALAR RASH



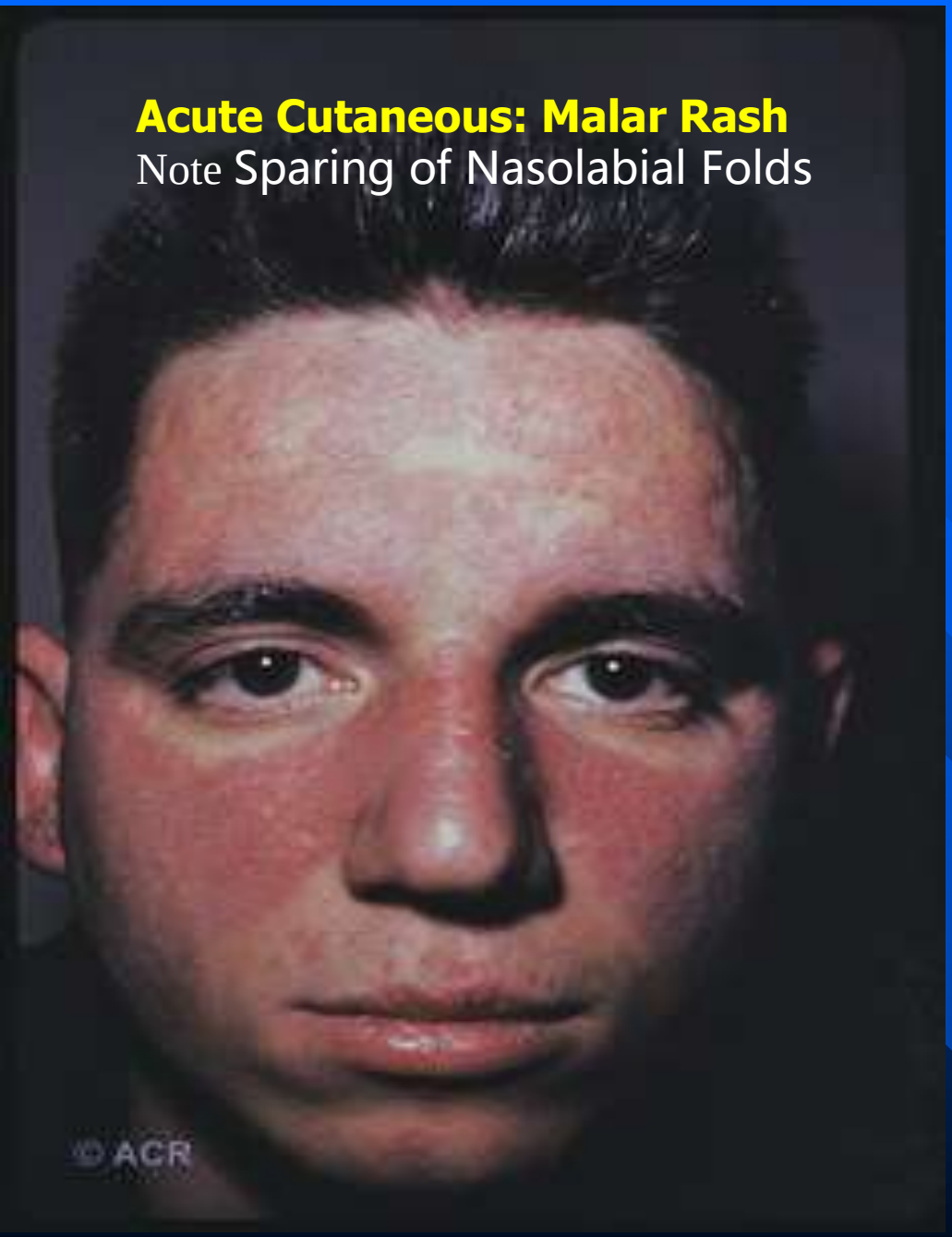
- Fixed erythema, flat or raised, o
  the malar eminences
- Tending to spare the nasolabial folds

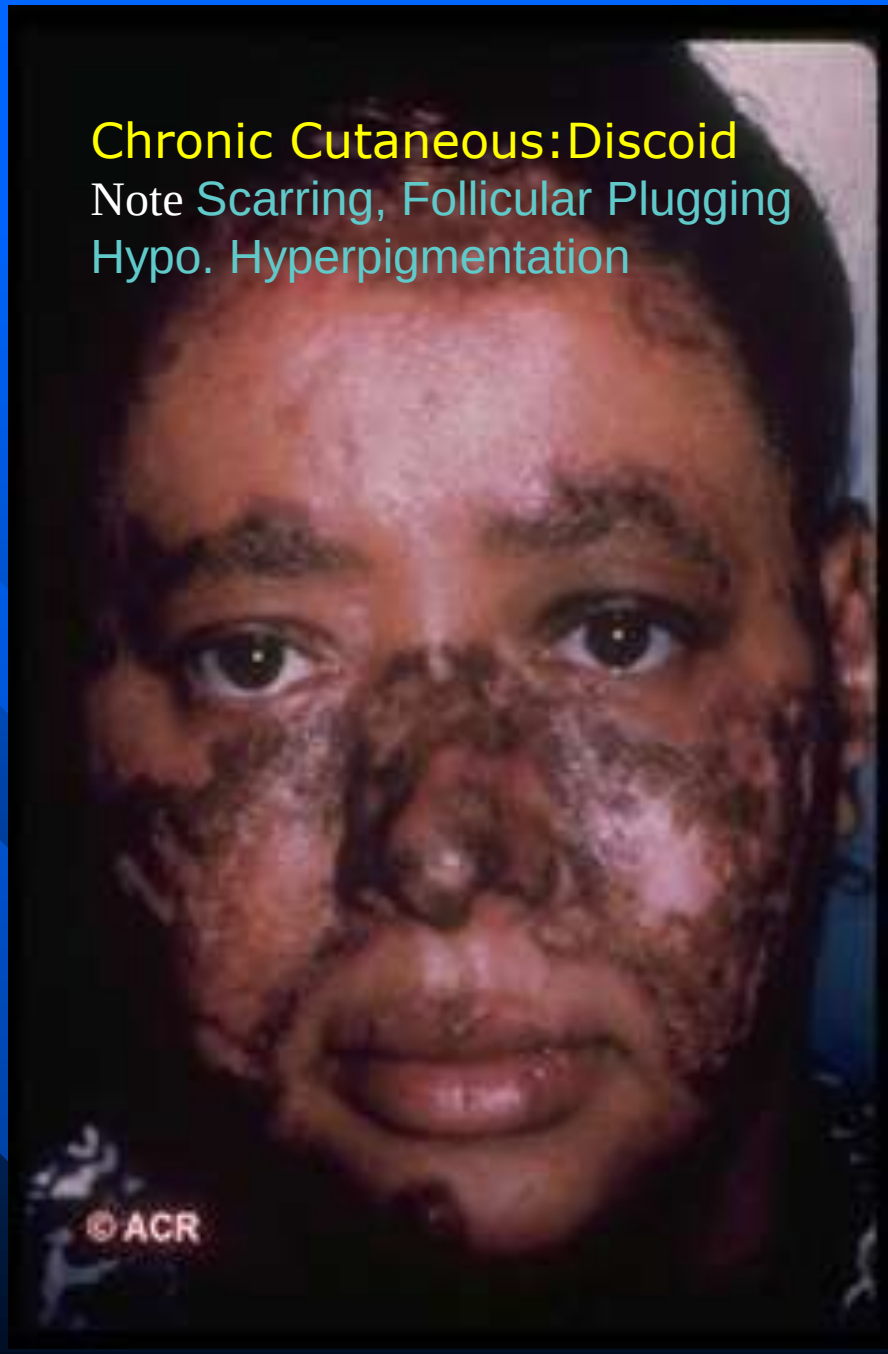




DISCOID RASH

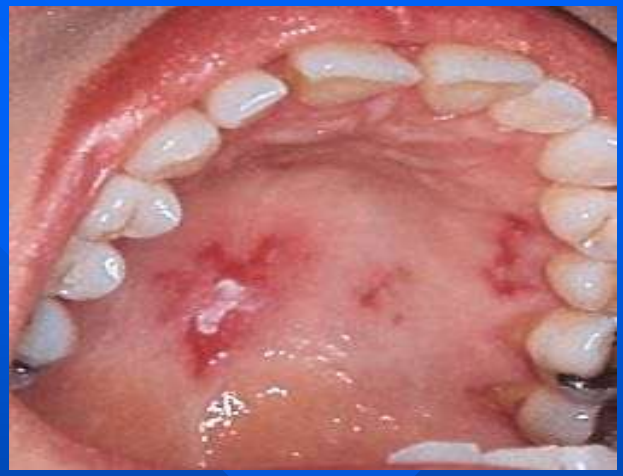
- Erythematous raised patches with adherent keratotic scaling and follicular plugging;
- Atrophic scarring may occur in older lesions

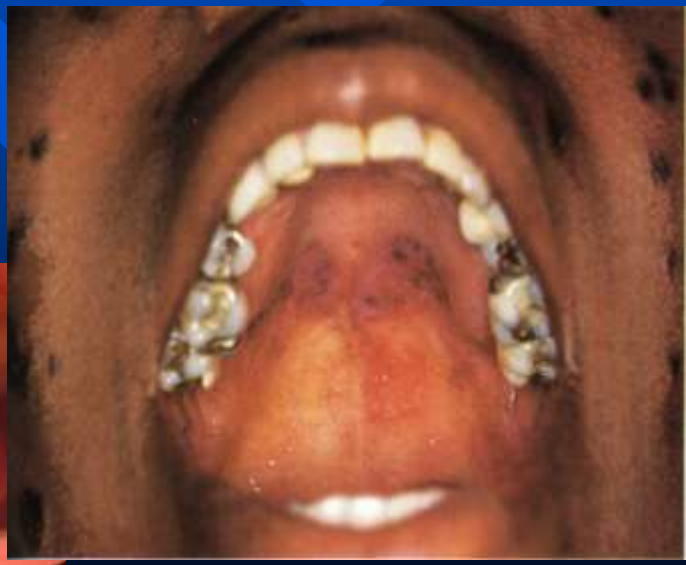

Acute Cutaneous: Malar Rash
Note Sparing of Nasolabial Folds
© ACR

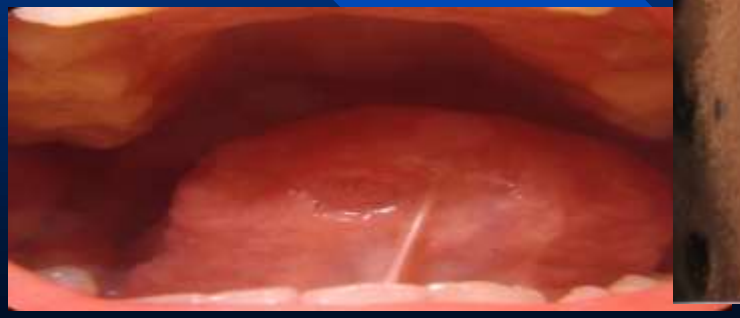

Chronic Cutaneous: Discoid
Note Scarring, Follicular Plugging
Hypo. Hyperpigmentation
© ACR

ORAL ULCERS

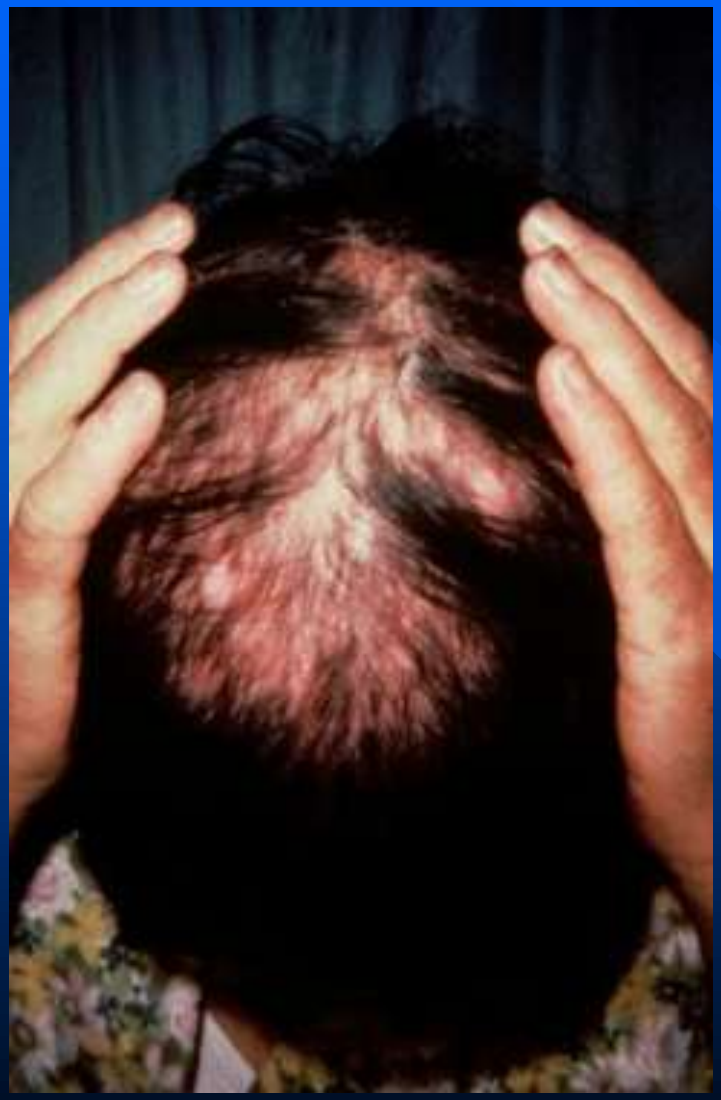
- Oral or nasopharyngeal ulceration
- Usually painless, observed by a physician



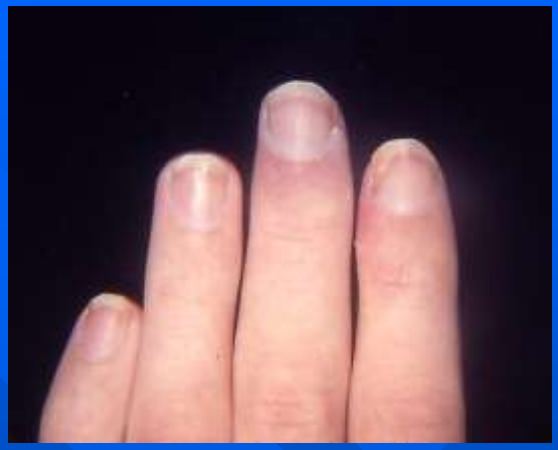




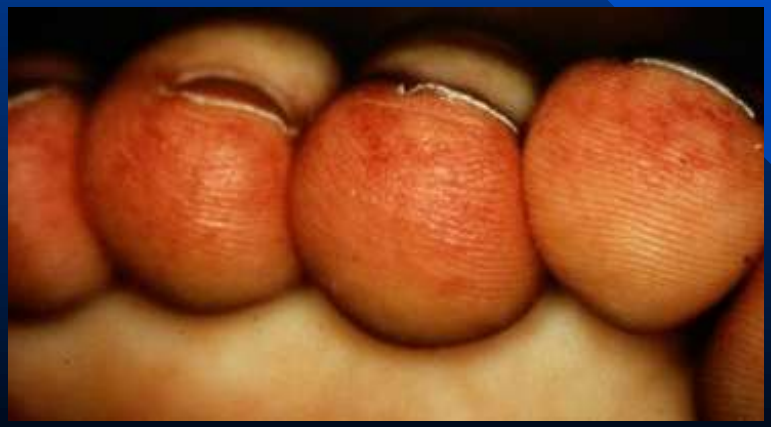
Scarring Alopecia, Follicular Plugging

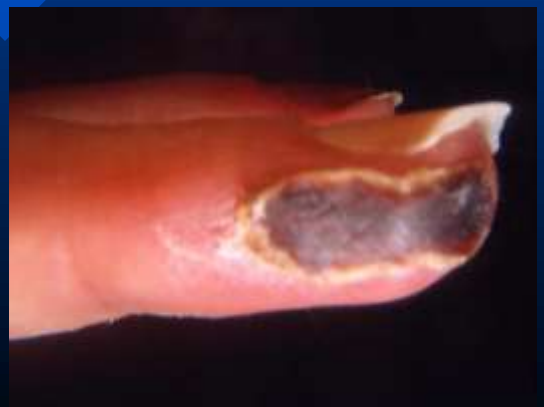


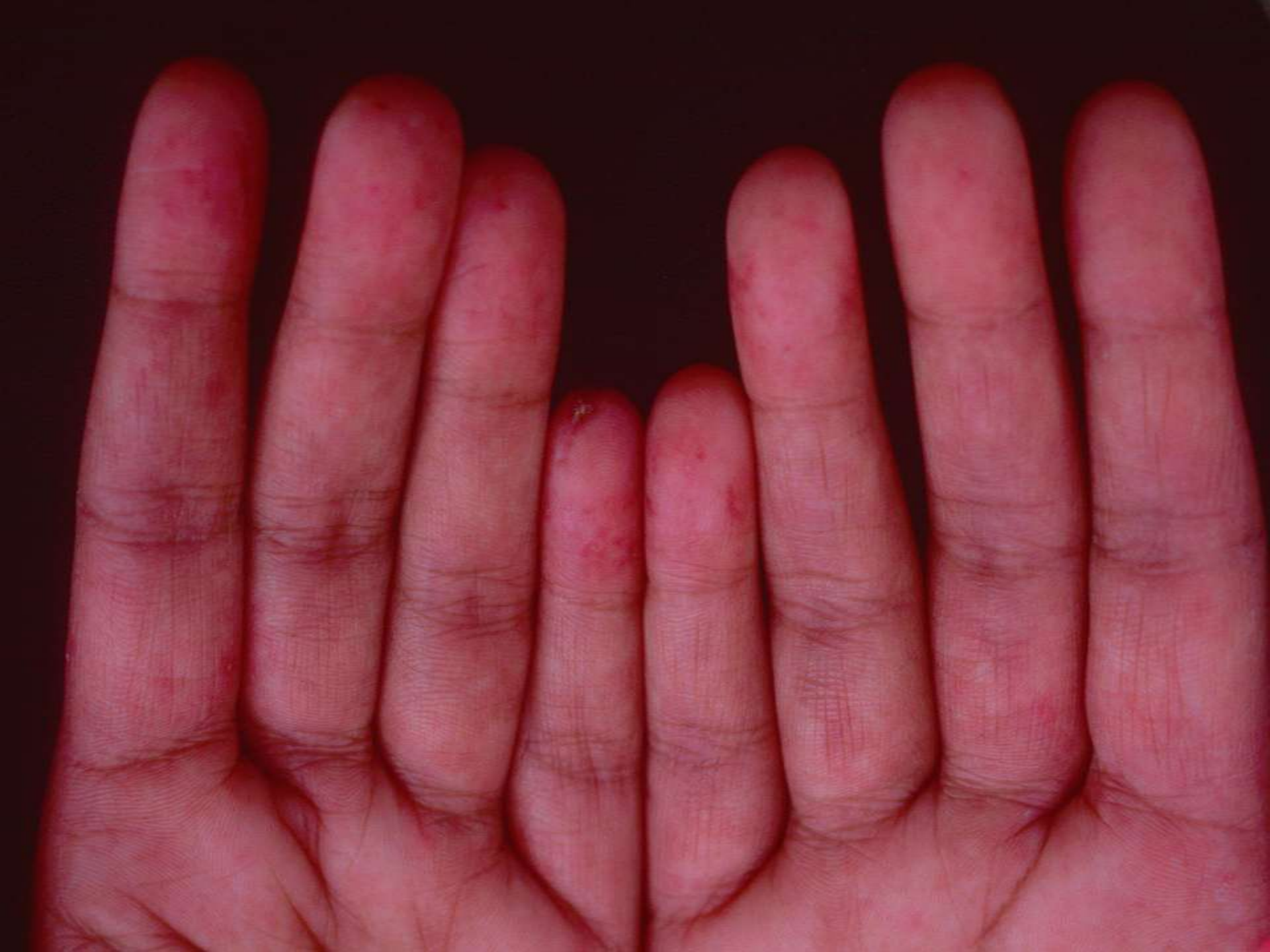
SLE - VASCULOPATHY



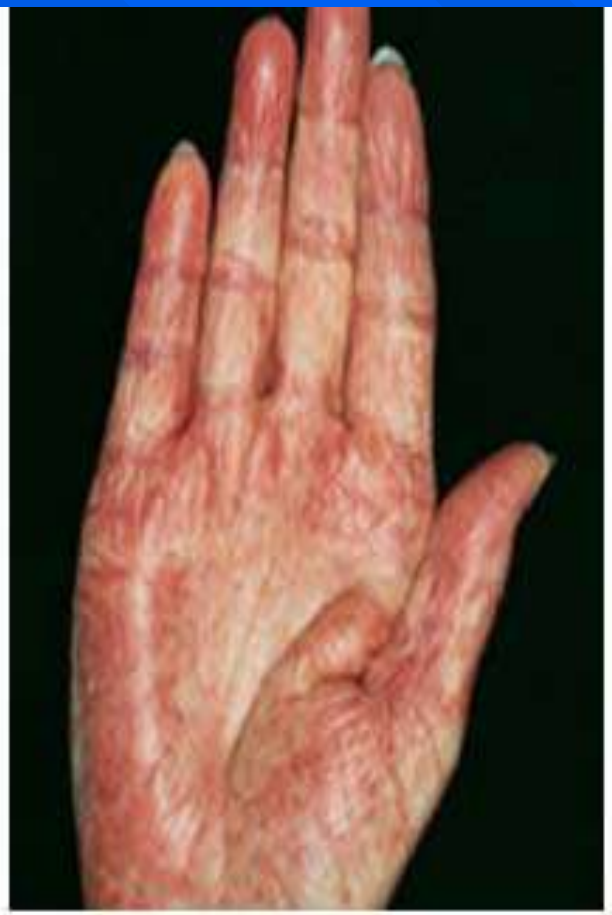
- Small vessel vasculitis
- Raynaud's phenomenon
- APL antibody syndrome







Palmar erythema



lsevier 2004. Habif: Clinical Dermatology 4E - www.clinderm.com

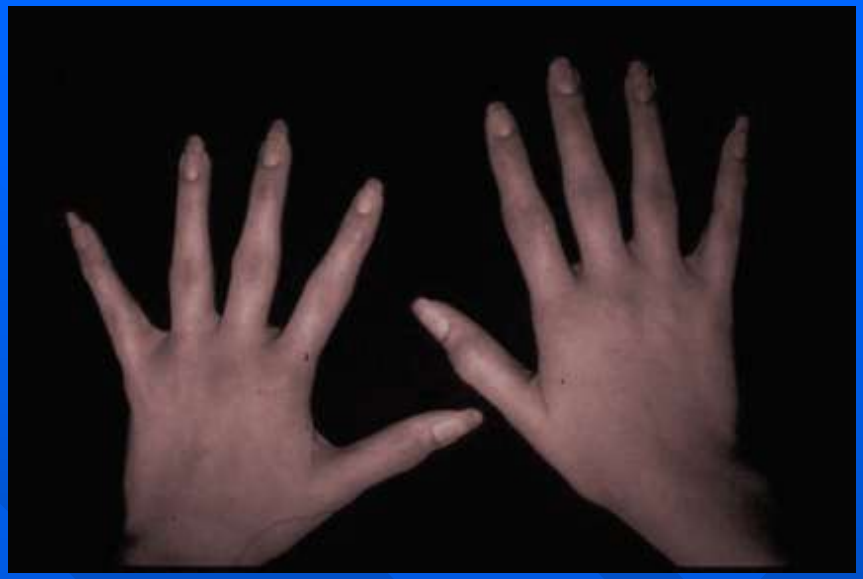
SLE (Cont'd)

- **The presence of vasculitis or urticaria in a patient with SLE is usually indicative of circulating immune complex disease and active, often severe, systemic involvement.**

Other clinical features

Arthritis

*a*rthralgia , myalgias



symmetrical, non-

erosive synovitis

typically of *small joints* of hands, wrists,& *knees*

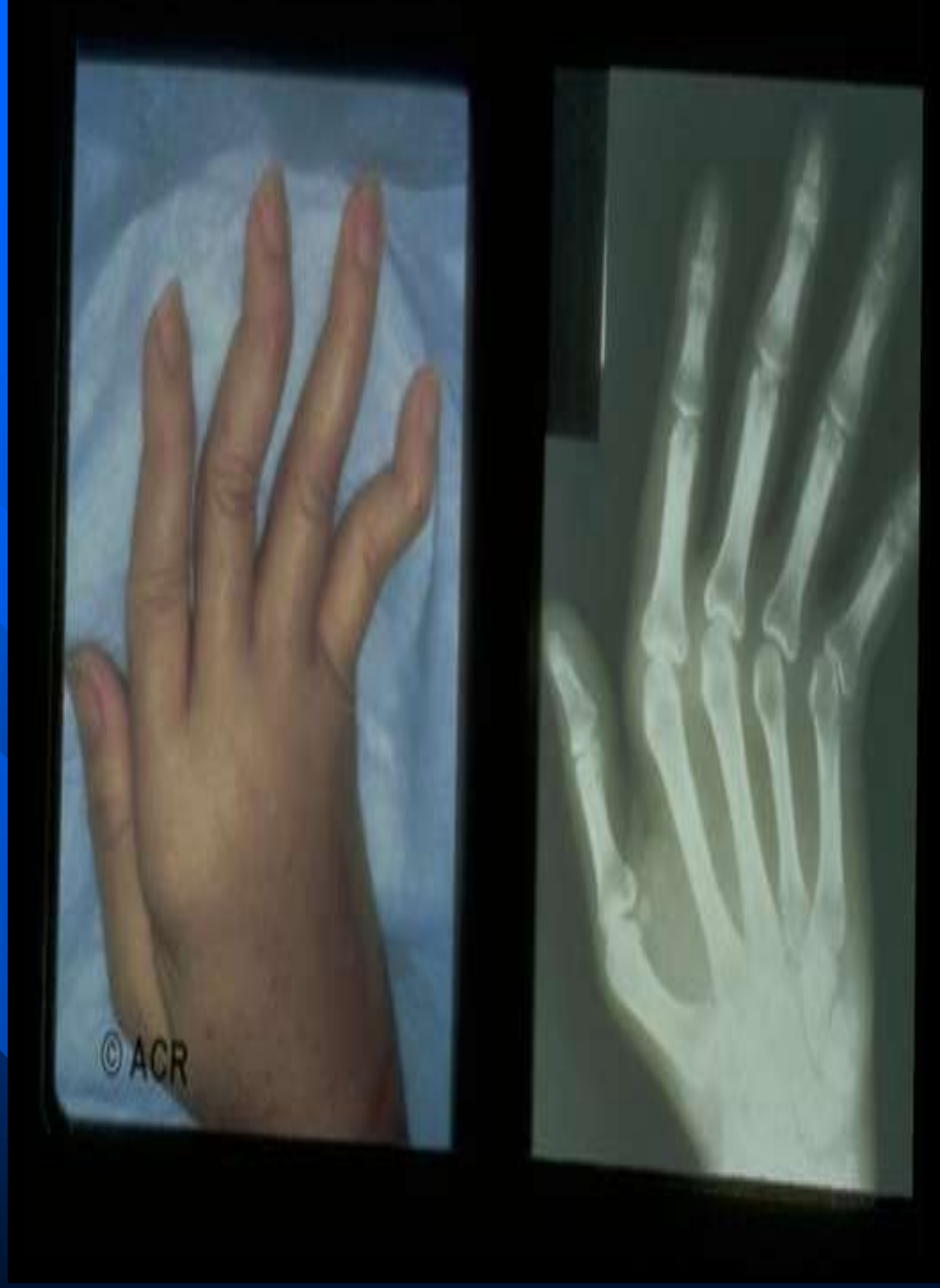
- Jacoub's arthropathy

formities)

sible

Arthritis(Jaccoub's Arthopathy)

- Most common
- Nonerosive, Reducible Deformities
- Transient, symmetrical,
- small joints



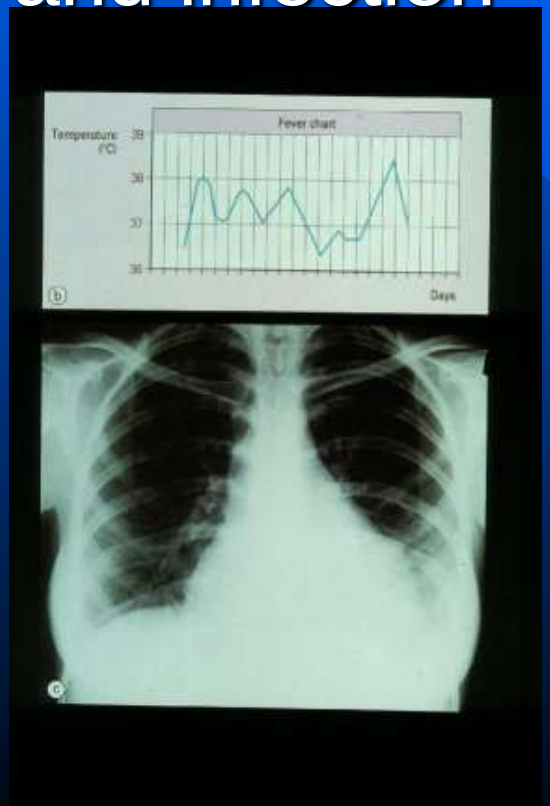
Pulmonary features

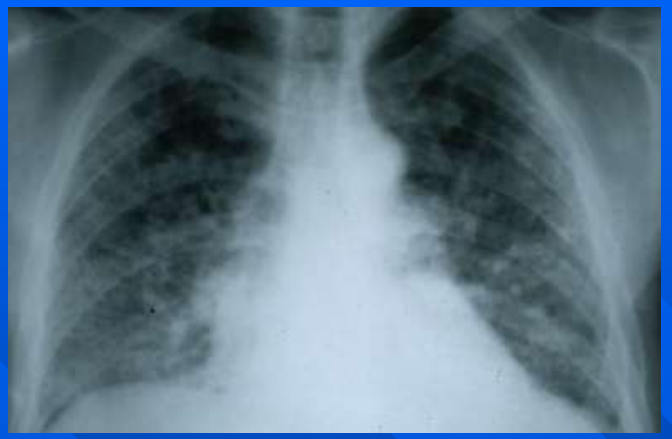
pneumonitis/fibrosis or haemorrhage

pleurisy commonest

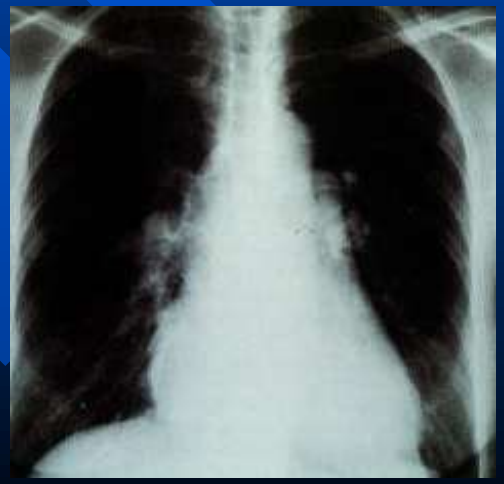
-consider also PE

and infection





pulmonary hypertension

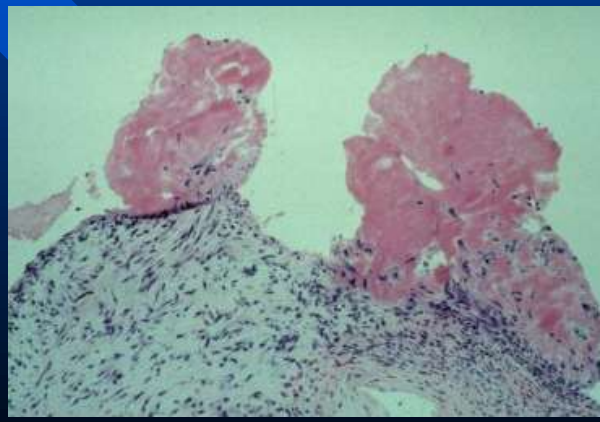


Cardiac manifestations

Pericarditis commonest

Myocarditis

Libman-Sacks endocarditis

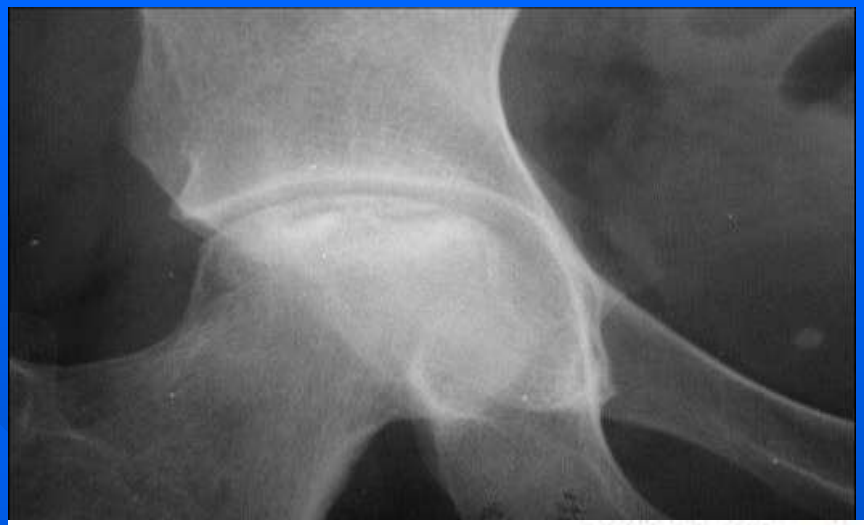


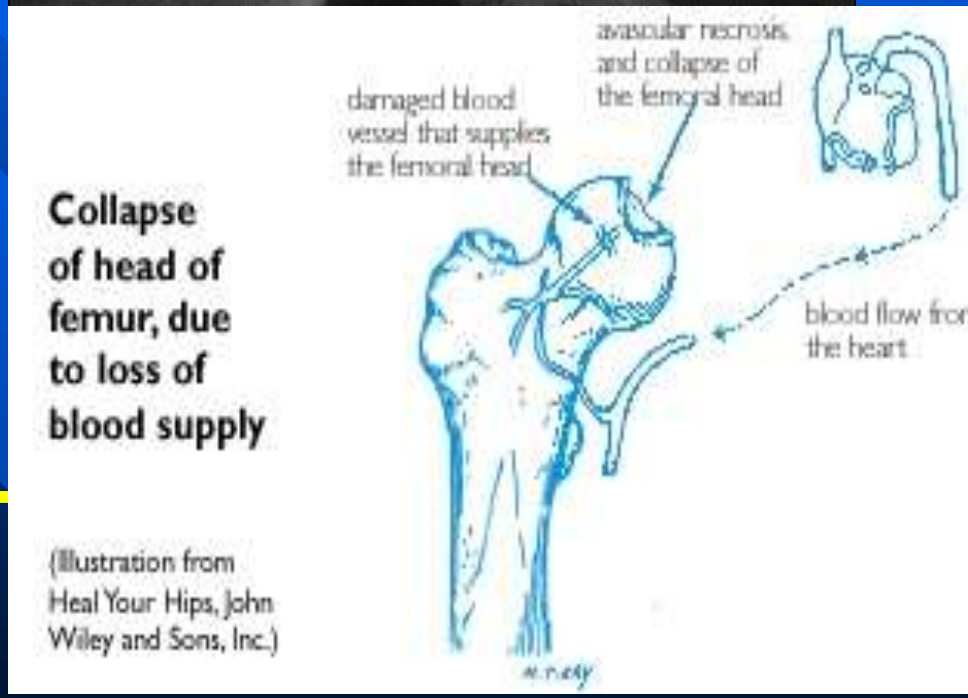
Coronary artery disease (premature)

Musculoskeletal

- Synovitis-90%
- Osteoporosis

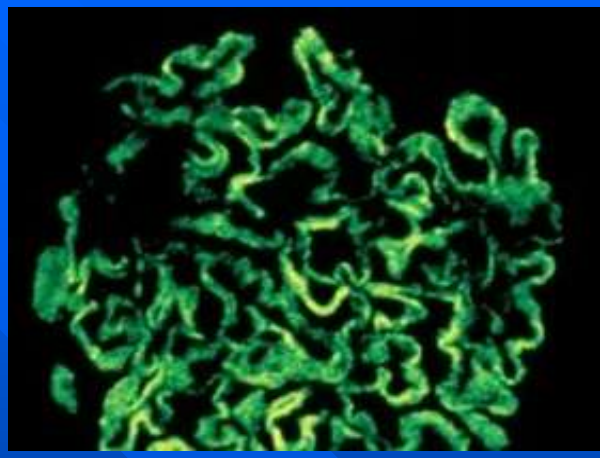
- Osteonecrosis (avascular necrosis)
-SLE itself or Cs T





Renal disease- consider biopsy if:

- Proteinuria > 0.5 g/24 hours
- red or white cells in urine
- casts
- creatinine clearance reduced (<80ml/min)



Gastrointestinal disease- (drugs?)

- anorexia, nausea, (vomiting)
- malabsorption or vasculitis/ischaemia

Typical neurological syndromes

Headache

Cerebrovascular disea

Seizure

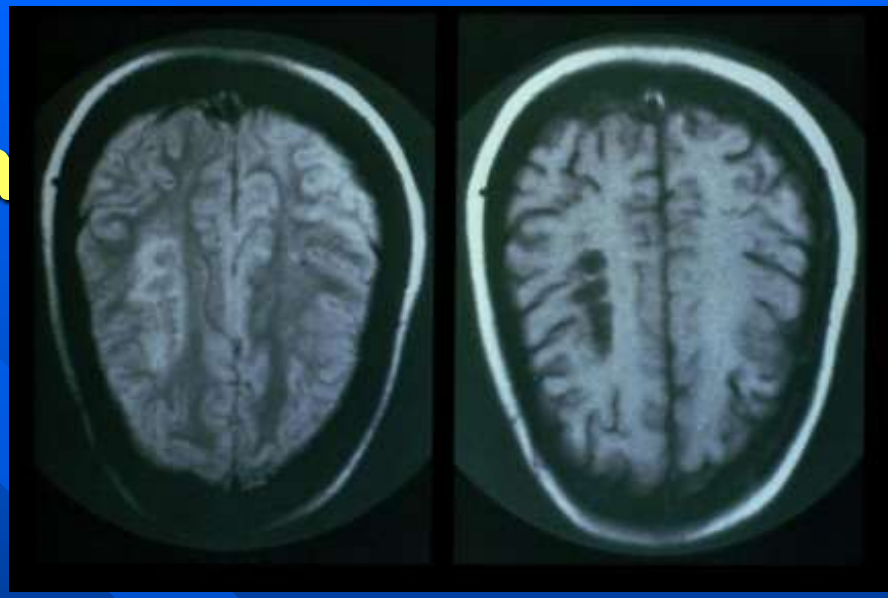
Chorea

Cognitive dysfunction

Psychosis

Mononeuropathy (single/multiplex)

Polyneuropathy



Reproductive features of SLE

- Recurrent Miscarriages
- Fetal growth retardation

- Neonatal lupus syndrome
- Congenital heart block

- Premature menopause

HEMATOLOGIC DISORDER

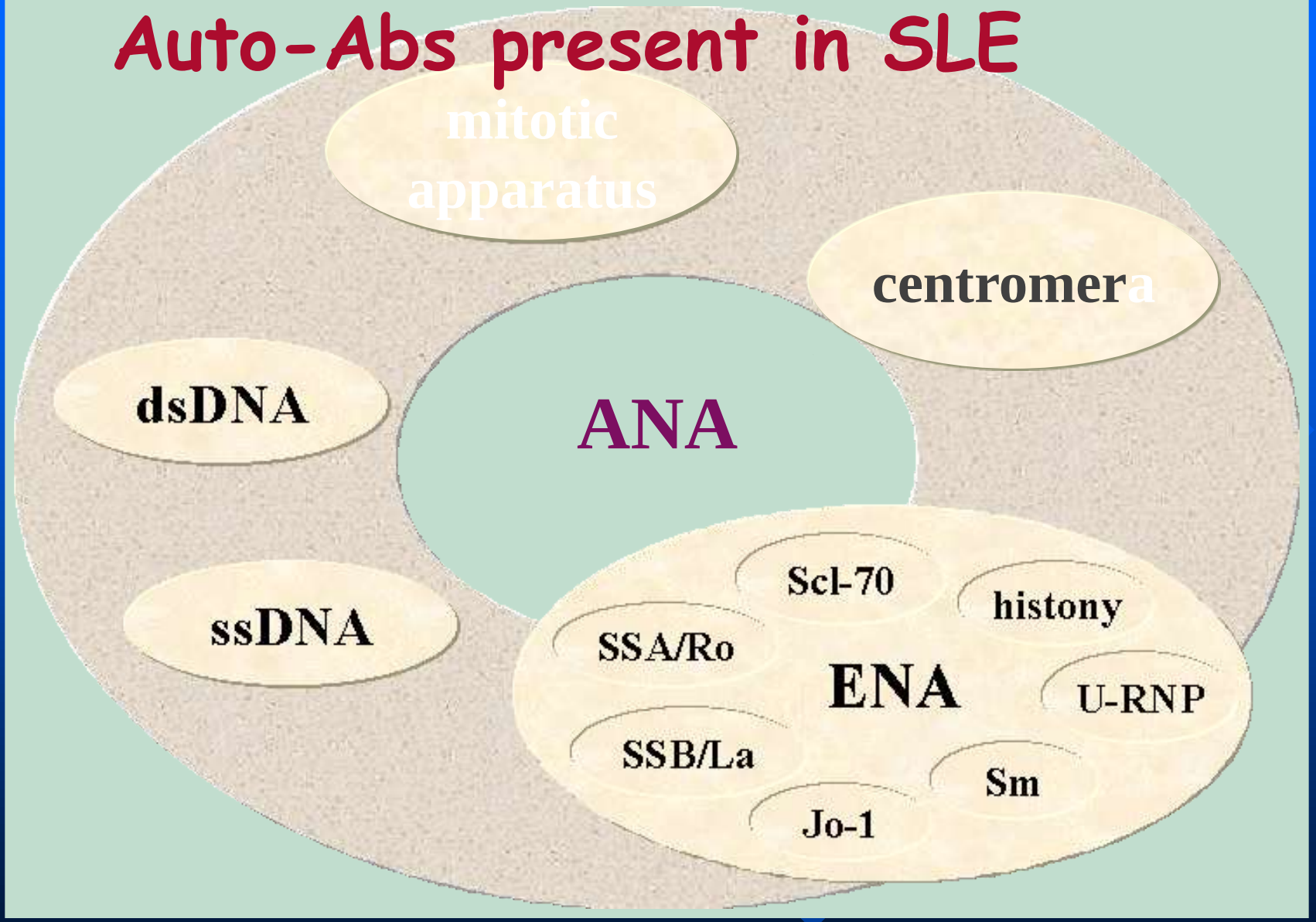
A) Hemolytic anemia - with reticulocytosis

B) Leukopenia < 4,000/mm^3 total on 2 or more occasions

C) Lymphopenia < 1,500/mm^3 on 2 or more occasions

D) Thrombocytopenia < 100,000/mm^3 (no offending drugs)

Auto-Abs present in SLE



ENA: extractable nuclear antigens

Lupus serology

ANA	Highly sensitive for SLE (+ in 98%)
	<u>Highly specific for SLE</u>
dsDNA	Lupus nephritis
Sm	severe SLE(20%)
rRNP	CNS lupus
	<u>Low specificity for SLE</u>
ssDNA	Risk of SLE in DLE pts, linear scleroderma
Histones	Drug-induced LE, localized scleroderma
U1RNP	MCTD
SS-A (Ro)	SCLE, Sojogren's, neonatal lupus
SS-B (La)	Sjogren's SCLE
APL / LA	Positive in 40% SLE

ANA

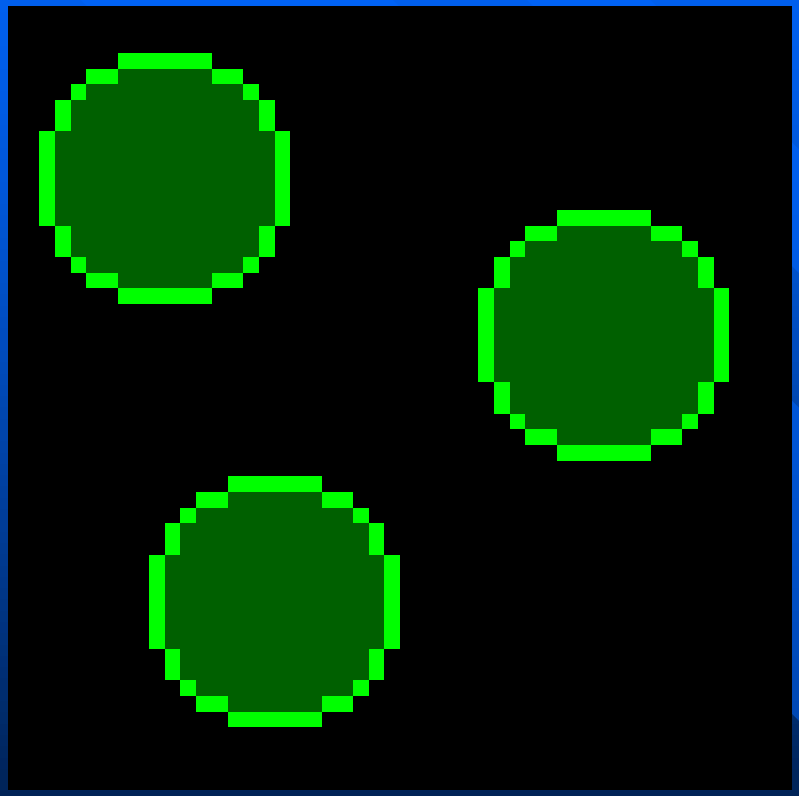
- It is useful as Screening test not prognostic nor follow up SLE or other CTD.
- False positive results in:

* 5-10 % of healthy individuals. .
* some pts with +ve family history of SLE.

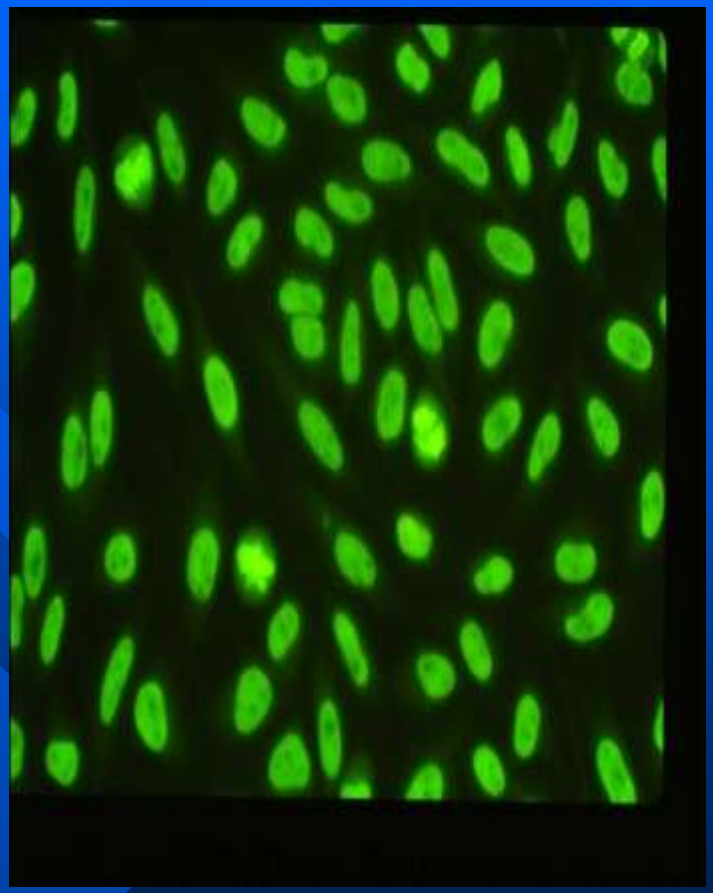
transiently positive in response to:

*viral infection.
*chronic infection.
lymphoproliferative disorders. *
*liver disease.
*

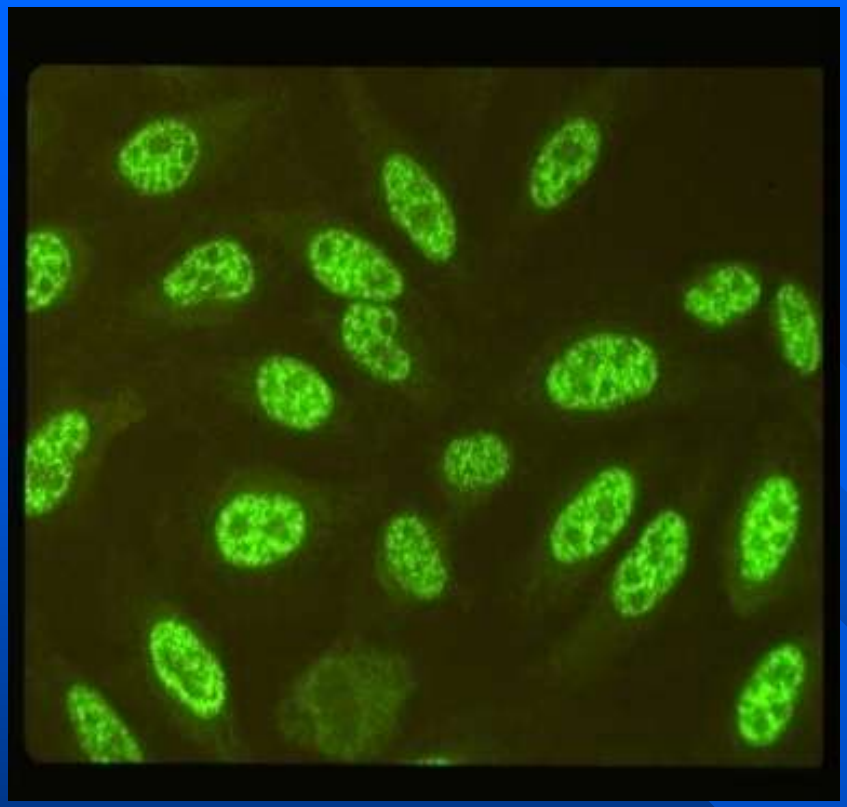
ANA Patterns



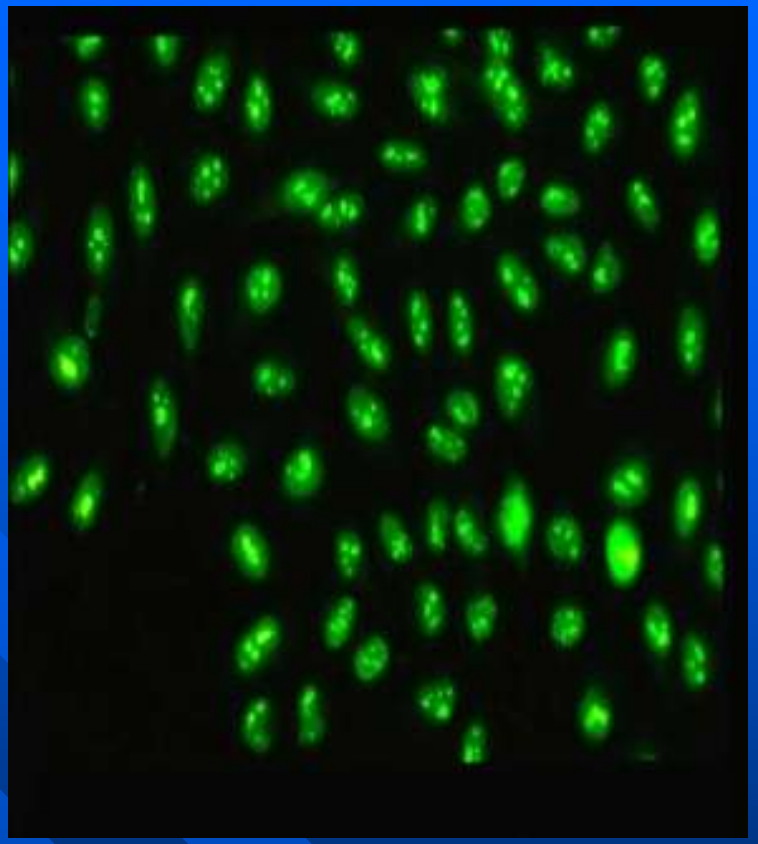
Peripheral Pattern (DNA)



Homogeneous Pattern
(Anti Histone AB)



Specled Pattern (Anti Smith, RNP, SS-A, SS-B, Jo-1, Scl-70)



Nucleolar Pattern (Nucleolus-specific RNA in Scleroderma)

Fluorescent ANA test (indirect IF)

	ANA	Antigen	Diagnosis	Prognosis
	Peripheral	nDNA	SLE	Poor
	Homogeneous	Histones nDNA	Drug-induced LE	Good Poor
	Nucleolar	Nuclear RNA	SLE PSS, SLE	Poor
	Centromere	Kinetochore	CREST	Good
	Speckled	ENA: SM RNP	SLE MCTD	Poor Good

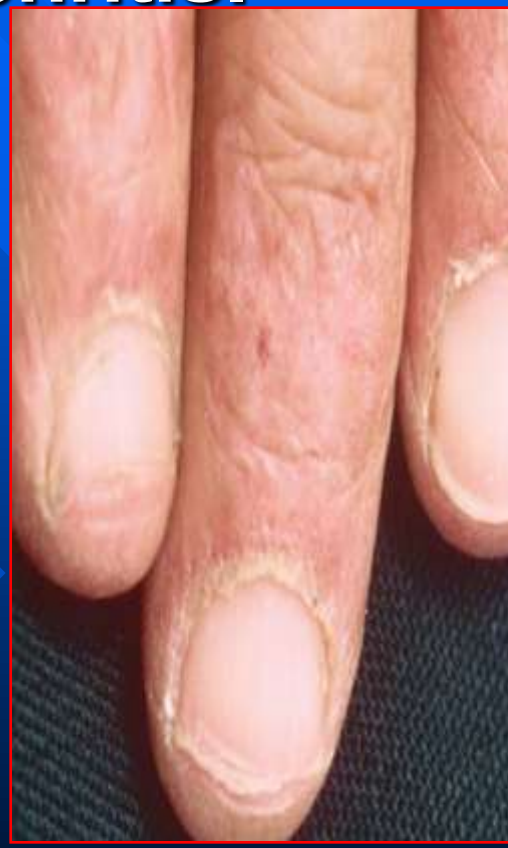
MARKERS FOR SLE:

- **ANA -ve exclude SLE except..**
- **ANA +ve +Anti-ds-DNA= SLE + lupus nephritis.**
  - **Specific not Sensitive (50-60-% SLE),**
    so its absence should not exclude SLE
- **SS-DNA in 70% SLE pts (lupus nephritis).but not specific to SLE (in RA & chronic infection)**
- **The titer increase with flares &is helpful in monitoring success of TTTof SLE**
- **ANA +ve + Anti-rRNP= SLE + CNS lupus**

MARKERS FOR SLE:

- **Anti- Smith antibodies:**

severe SLE with mebranous nephritis.



- **Anti- RNP Abs:**

-- mild SLE .

-MCTD (High titer) .

-Sjogron $

- **RA, scleroderma**

- **APL *Abs* = thrombotic risk &**
- **recurrent spont abortion in women**

MARKERS FOR SLE:

- **Anti-SSA (RO) Abs:**
  - -mild SLE -SCLE
  - - Neonatal LE -Sjogren's $
- **Anti- SSB(La) Abs:**
  - - SLE patients
  - - Sjogren's $(60%) .
- **Anti-histones:**

  Drug Induced LE

REVISED ARA-CRITERIA FOR SLE DIAGNOSIS 1982

1. **Malar rash**
2. **Discoid rash**
3. **Photosensitivity**
4. **Oral ulcers**
5. **Arthritis**
6. Polyserositis
7. **Renal disease**.
   - > 0.5 g/d proteinuria
   - ≥ 3+ dipstick proteinuria
   - Cellular casts
8. **Neurologic disease.**
   - Seizures
   - Psychosis (without other cause)
9. **Hematologic disorders.**
   - **Hemolytic anemia**
   - **Leukopenia (< 4000/uL)**
   - **Lymphopenia (< 1500/uL)**
   - **Thrombocytopenia (< 100,000/uL)**
10. **Immunologic abnormalities**.
    - **Positive LE cell**
    - **Anti-ds- DNA** **Anti- Sm**
    - **Any APL**
11. **Positive ANA (95-100%)**

CLASSIFICATION CRITERIA

- Must have 4 of 11 for Classification
  - Sensitivity 96%
  - Specificity 96%
- However, diagnosis is ultimately **clinical**
- Not all “Lupus” is SLE
  - Discoid Lupus
  - Subacute Cutaneous Lupus
  - Drug induced lupus
  - Overlap syndrome

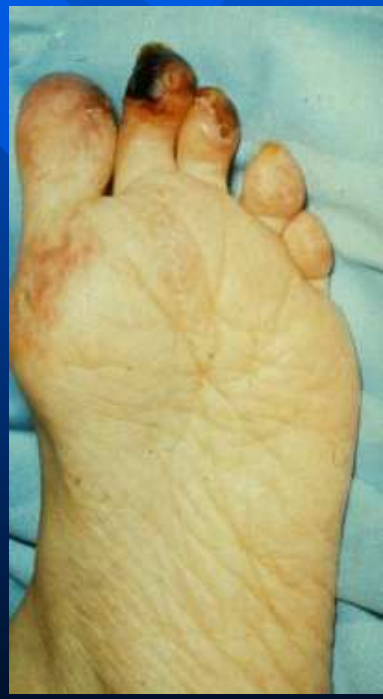
- When you see cutaneous signs of lupus…
  - •Referral to a Rheumatologist is helpful

- Communicate with relevant colleagues
- • Evaluate as a team for internal manifestations
- • Match the best therapy to the presumed skin/internal manifestations the


Is it over yet?

LUPUS RELATED SYNDROMES
Antiphospholipid Syndrome (APS)

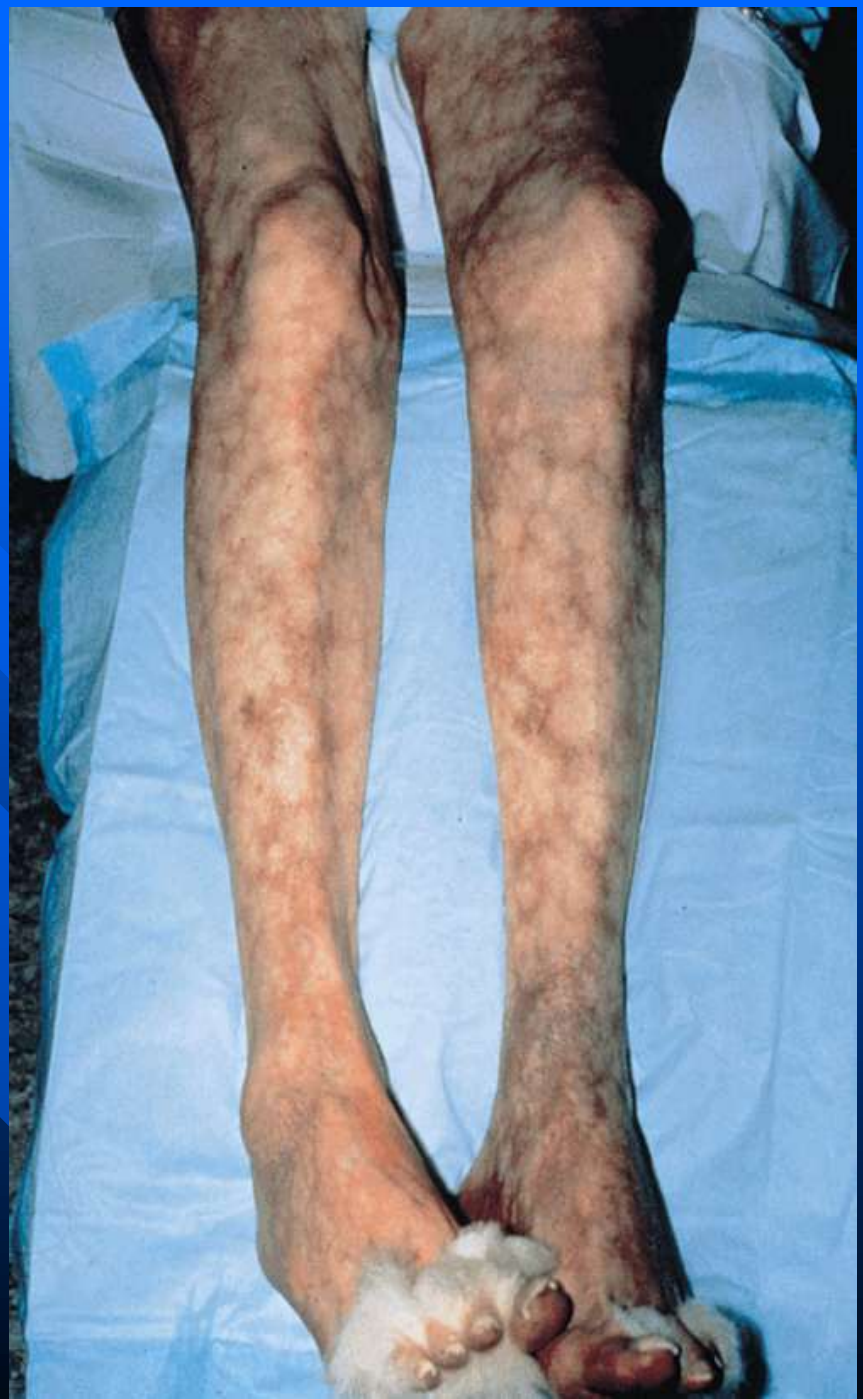
- Recurrent venous & arterial thrombosis
- **Antiphospholipid antibody**
  - **LAC-Abs to coagulation factors.**
  - **Prolonged aPTT**
  - **Anti-cardiolipin**
- **Depressed serum complement**
- **Anti histones Abs**



C/P

- Livedo Reticularis
  - Pregnancy: Recurrent abrtion in first trimester
  - Primary (no other SLE feature) or Secondary (SLE features present).

ACR



Raynaud's Syndrome

-Not part of the diagnost
criteria for SLE

- Does NOT warrant ANA if n
clinical evidence

In MCTD:

- , sclerodactyly, arthralgia,
- +ve nRNP Abs

Raynaud's phenomenon

IV-SJÖGREN'S SYNDROME

1- ANA in 70% of patients.

2-Anti-SSA (RO) Abs :

- in 50 - 70% of Sjogren's syndrome.

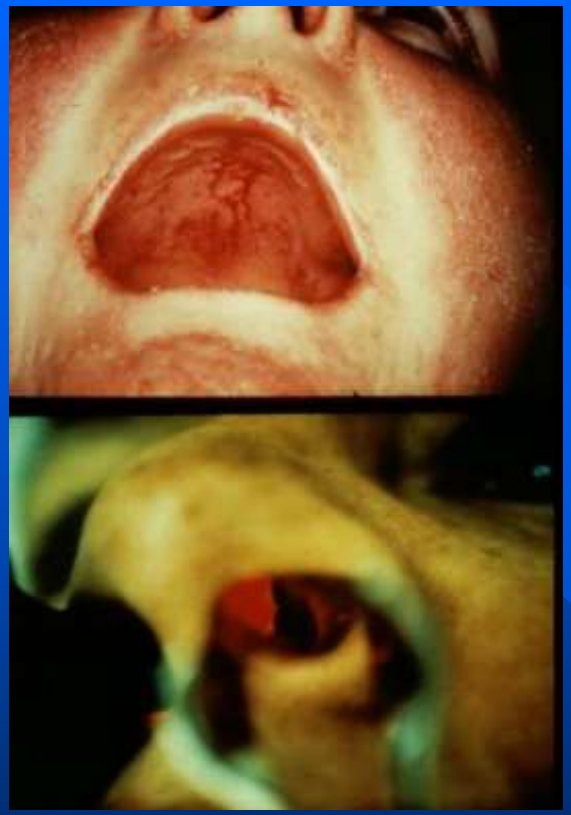
3-Anti- SSB(LA) Abs:

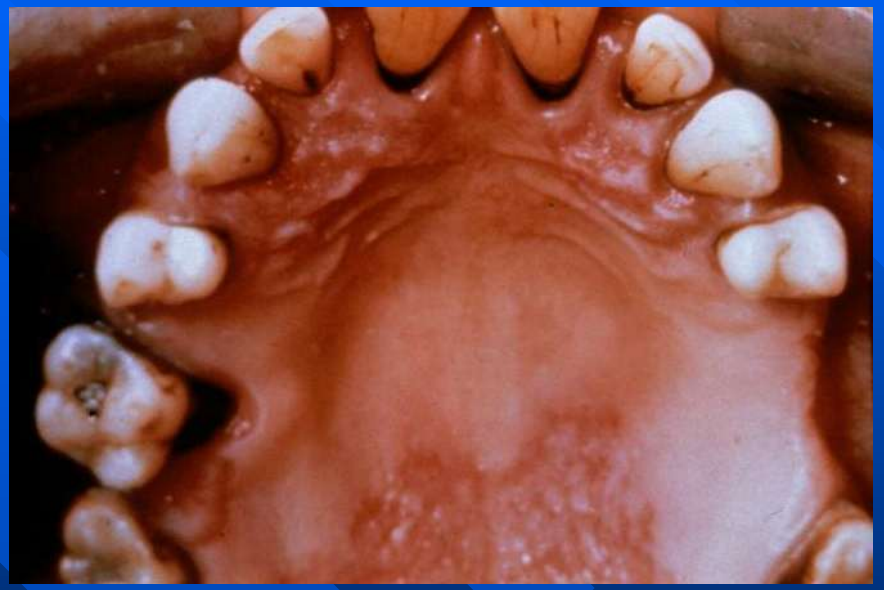
- in 60% of Sjogren's syndrome

4-RF in 90% of patients.

.

Mucosal ulcers in **Sjogren's syndrome**





Sicca symptoms- secondary Sjogren's syndrome

Drug Induced Lupus

- +ve ANA
- Male:Female ratio is equal
- Nephritis and CNS abnormalities rare
- No anti-DNA Abs
- Normal C3,C4
- Classically associated with hydralazine, isoniazid, procainamide
- Symptoms usually resolve with stopping drug

Comparison of drug-induced SLE & SCLE

	SLE	SCLE
• Skin lesions	• Rare	• SCLE or gyrate erythema
• Serositis	• Common	• Occasional
• Serology	• Anti-histone	• Anti-Ro(SS-A)
• Drug	• Procainamide, hydralazine, minocycline, INH,anti-TNF agents, etc.	• HCTZ, Ca channel blockers, terbinafine, ACE inhibitors, statins, anti-TNF agents, etc.

Thank you

Questions or Comments?

Q -ANA is useful in evaluating:

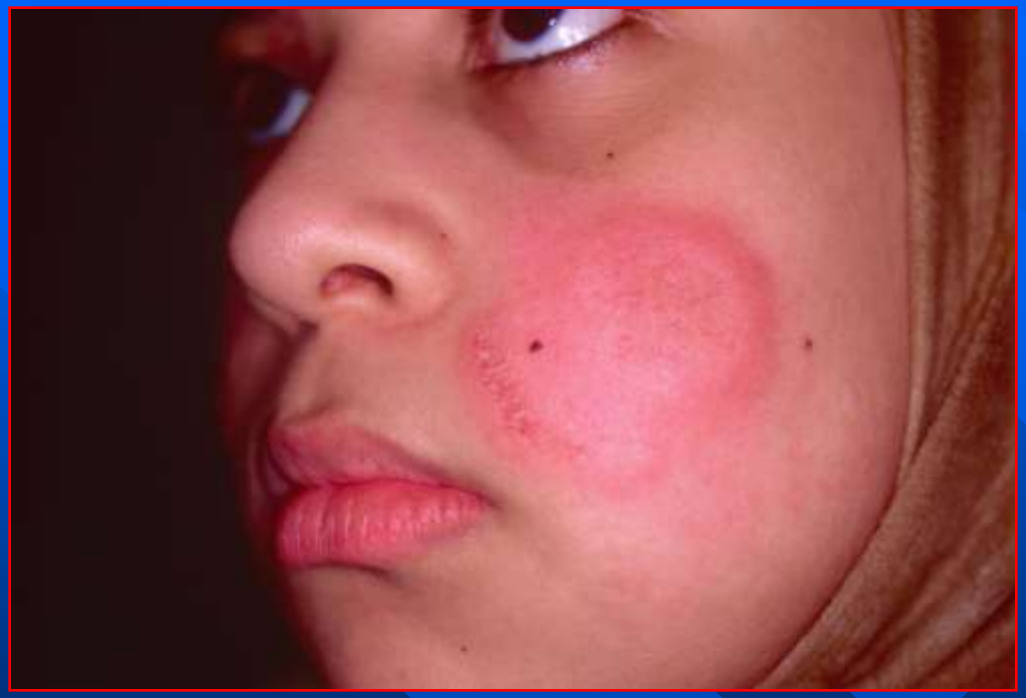
a) Patients with photosensitivity.

b) Patients with chronic vasculitis.

c) Patients undergoing phototherapy.

d) Patients with facial eruptions.

e) Patients with discoid LE.



الرقم المعملى : 127937

تاريخ الحضور: 2003/08/07

تاريخ الإستلام: 2003/08/12 الساعة 9:30 مساءا

Immunology Unit

		Ref. Range	
Anti DNA by ELISA	**Negative 17** AU/mL	Up to 26-	
Ro (SS-A).	**Positive 73** Units	< 20	Negative
		20-39	Weak pos.
		40-80	Mod. positive
		> 80	Strong pos.
La (SS-B)	**Positive 178** Units	< to 20	Negative
		20-39	Weak Pos.
		40-80	Mod. Positive
		>80	Strong Pos.

Which of the following drugs has been linked to both drug-induced SLE & drug-induced SCLE? 1. (d)

a) Terbinafine.

b) Hydrochlorothiazide.

c) Etanercept.

d) Minocycline.

In comparison to SLE, which of the following is statistically more frequent in SCLE?

(a)

a) Photosensitivity.

b) Renal disease.

c) Anti-Ro / SS-A antibody.

d) Leukopenia.


واجتمع العظماء فى جمهورية طرة العظمي

Thank you

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